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LETTERS AND CORRESPONDENCE

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Spontaneous Regression of Diffuse Large-Cell Lymphoma Associated With Hashimoto's Thyroiditis

To the Editor: As reviewed by Gattiker et al. [1], spontaneous regression (SR) of diffuse large-cell lymphomas is rare. We experienced SR of diffuse large-cell lymphoma arising on extranodal sites.

A 68-year-old female was admitted because of bilateral thyroid masses in April 1993. Laboratory findings included leukocytosis, elevated CRP, and LDH. Thyroid hormone was low, with increase of TSH and anti-microsome antibody titer. Needle biopsy of the left thyroid revealed diffuse infiltration of small-to-medium-sized lymphoid cells with cleaved nuclei (Fig. 1a). Inflammatory changes existed, with scattered multilobulated or multinucleated giant cells (Fig. 1b). The pathological diagnosis was strongly indicative of non-Hodgkin's lymphoma (NHL). For definitive diagnosis, whole left-lobe resection was performed. Histology exhibited a cluster of medium-to-large-sized lymphoid cells (Fig. 1c, surrounded by arrows), with cleaved nuclei associated with lymphoepithelial lesion (Fig. 1d, arrow) on the background of Hashimoto's thyroiditis (Fig. 1c). The lymphoid cells in the cluster were selectively stained with anti-κ monoclonal antibody. The pathological diagnosis was NHL, diffuse mixed type in the Working Formulation [2]. However, after resection, the tumor in the right lobe disappeared spontaneously.

Two months later, the patient noticed subcutaneous tumors at the left breast and lower back. Laboratory data showed leukocytosis. The pathological diagnosis of the breast tumor was NHL, diffuse large-cell type (Fig. 1e). κ-restricted expression was again demonstrated by immunohistochemistry. Surprisingly, the tumors in her back disappeared spontaneously within 2 weeks after biopsy.

In late November, she was readmitted with dyspnea and multiple subcutaneous nodules. Leukocytosis, elevated CRP, and remarkably high LDH (2,987 IU/l) were observed. The pathology was again NHL, diffuse large-cell type (Fig. 1f). Southern blot analysis detected monoclonal gene rearrangements of IgH and Igκ. CT scan demonstrated involvement of the lung and bilateral adrenal glands. In spite of systemic involvement, she was successfully treated with conventional chemotherapy and remains in complete remission.

In our case, lymphoma first appeared in the thyroid and seemed to be mucosa-associated lymphoid tissue (MALT) lymphoma, considering the background of Hashimoto's thyroiditis [3]. Histology was also compatible to low-grade MALT lymphoma [3]. Therefore, SR of the thyroid lymphoma alone is not very surprising. However, the disappearance of diffuse large-cell lymphoma of subcutanea is unusual. Although histology is quite different, κ light-chain restriction and sites of involvement (always extranodal) suggest the clonal identity. Extranodal lymphoma of MALT type has been classified as a distinctive category in a revised European-American classification of lymphoid neoplasms (REAL classification) because of its favorable clinical feature in contrast to its nodal counterpart [4]. The clinical course of our case may indicate the MALT lymphoma's character even after transformation to a higher grade, and may demonstrate the importance of lymphoma-originated sites.

Although the cause(s) of SR is not well-understood, association of acute inflammation has been described [5,6]. In our case, appearance and SR of lymphomas were always accompanied by inflammatory signs, suggesting the importance of inflammatory reactions for SR.

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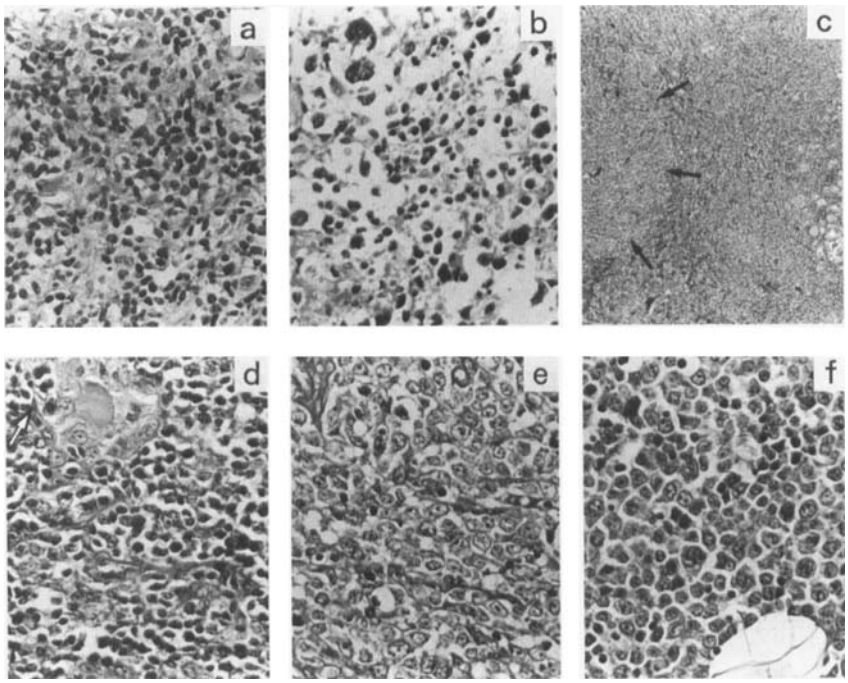

Fig. 1. Histopathological features of biopsy specimens. a, b: Needle biopsy of left thyroid tumor. a: Infiltration of lymphoid cells. b: Giant cells in edematous stroma, with inflammatory changes such as neutrophils and nuclear debris. c: Open biopsy of left thyroid lobe; a focus of lymphoma cells are observed at left (surrounded by arrows), in background of Hashimoto's thyroiditis. d: Higher magnification of lymphoma focus in c, with lymphoepithelial lesion (arrow). e: Tumor in breast at first relapse. f: Subcutaneous nodule at second relapse (H&E stain).

Detection of α-Thalassemia-2 (−3.7 kb) and Its Corresponding Triplication ααα (Anti-3.7 kb) by PCR: An Improved Technical Change

To the Editor: In 1994 we published in this journal [1] a PCR procedure for the detection of the two most common types of α-thalassemia-2, namely, the 3.7-kb and 4.2-kb deletions. This method has since then been used by us and many laboratories around the world with considerable success. Quite a few investigators, however, have experienced some "aspecific" amplification products that have also been observed in our own experiments (Fig. 1, left), and that may interfere with the detection of the 3.7-kb deletion. The reason for the occurrence of these smaller fragments is not clear. In order to avoid this problem we have developed a new set of primers and have used these for more than 1 year for detection of the α-thalassemia-2 (3.7-kb) deletion as well as the ααα (anti-3.7-kb) triplication, without any further complications. The amplification products for the normal, the −3.7-kb allele, and the triplication allele are 1.76 kb long [2], and additional bands have not been observed (Fig. 1, right).

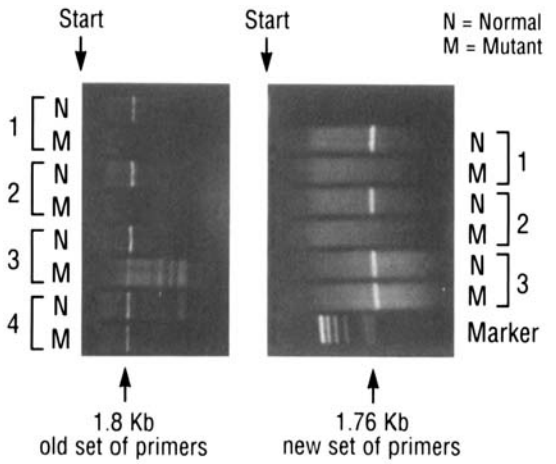

Fig. 1. Detection of 3.7-kb α-thalassemia-2 deletion by PCR. Left: Old procedure; occasionally, smaller-sized amplification products are observed. Right: Similar data with new primer set. Samples 1 and 2, normal (αα/αα); samples 3 and 4; α-thalassemia-2 (−3.7 kb) heterozygote (αα/−α).

Technical details for the detection of the 3.7-kb deletion are as follows: common forward primer (positions +5671–+5695 in the α2 promoter), 5′-CCCTCCCCCTCGCCAAGTCCACCCC-3′; normal reverse primer (positions +7431–+7409 in the 3′UTR of the α2 gene), 5′-GGGAGGCC-CATCGGGCAGGAGGAAC-3′; and mutant reverse primer (positions +11254–+11231 in the 3′UTR of the α1 gene), 5′-GGGGGGAGGCC-CAAGGGGCAAGAA-3′ (positions are listed according to data from GeneBank HUMHBA4). Details for the detection of the ααα (anti-3.7-kb) triplication are as follows: forward primer (positions +9354–+9378 in the α1 promoter), 5′-CCCTCCCCGAGCCAAGCCTCCTCCC-3′; and reverse primer (positions +7431–+7409 in the 3′UTR of the α2 gene), see above.

The 10 × PCR "α" buffer consists of: 1 M Tris-HCl, pH 8.8, 3,350 μl; 1 M $MgCl_2$, 100 μl; 1 M ammonium sulfate, 830 μl; β-mercaptoethanol, 35 μl; bovine serum albumin (4%), 125 μl; and H_2O, 560 μl; final volume, 5,000 μl; the buffer can be kept at 4°C for 2–4 months. The reaction mixture (for two samples) consists of: H_2O, 87.2 μl; 10 × PCR "α" buffer,